

SUMMARY of PRODUCT CHARACTERISTICS

1. NAME OF THE HUMAN MEDICINAL PRODUCT

FLUIBRON[®] 15 mg/5 ml pediatric syrup

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredient:

5 ml (1 spoon) FLUIBRON[®] pediatric syrup contains 15 mg ambroxol HCl.

Excipients:

Contains sorbitol (E420) (2500 mg).

For excipients, see 6.1.

3. PHARMACEUTICAL FORM

Syrup.

Colorless, clear syrup.

4. CLINICAL CHARACTERISTICS

4.1. Therapeutic indications

In acute and chronic disorders of respiratory tract associated with thick and viscid mucus.

4.2. Posology and method of administration

Posology/frequency and duration of administration:

In children:

Between ages 0-2: 1/2 cup (2.5 ml) twice a day.

Between ages 2-5: 1/2 cup (2.5 ml) three times a day.

Between ages 5-12: 1 cup (5 ml) 2-3 times a day.

The doses may be doubled in the beginning of treatment. May be diluted with water or fruit juice.

Method of administration: Administered orally. May be diluted with water or fruit juice.

Additional information for special populations

Kidney/liver failure: Caution must be exercised in patients with kidney, liver diseases and peptic ulcer.

Pediatric population: For use in infants and children between 0 to 12 years of age, see "Posology/frequency and duration of administration" section.

Geriatric population: There are no special conditions for use in geriatric population.

4.3. Contraindications

Not used in persons, who are hypersensitive to bromhexine or ambroxol.

4.4. Special warnings and special precautions for use

- Must not be used with antitussives, such as codeine, which may prevent discharge of mucus or secretion inhibitors, such as atropine.
- Caution must be exercised in patients with kidney, liver diseases and peptic ulcer.
- Patients with rare hereditary fructose intolerance problem must not use this medication.

4.5. Interactions with other medicinal products and other forms of interaction

It has no interaction in particular with cardiac glycosides, corticosteroids, bronchodilators, diuretics and antibiotics. However, atropine and amantadine, showing antimuscarinic action, tricyclic antidepressants, haloperidol, antihistamines, other drugs, such as procainamide

(ipratropium) may decrease ciliary motility and mucociliary clearance and may cause accumulation of mucosa secretions.

Additional information for special populations

No interaction studies concerning special populations have been made.

Pediatric population: No interaction studies concerning pediatric populations have been made.

4.6. Pregnancy and lactation General recommendation

Pregnancy Category is B.

Women with childbearing potential/Contraception

There are no recommendations concerning the use of the drug in women with childbearing potential and women, who use contraceptives.

Pregnancy

Since adequate clinical studies are not available, in the first trimester of pregnancy, it may be used only in necessary cases, by making a benefit-risk assessment.

Lactation

It is not known whether ambroxol is excreted in human milk. Therefore, caution must be exercised in lactating women.

Fertility

Experimental studies have shown that the drug did not show teratogenic characteristics. For detailed information please see “5.3 Pre-clinical safety data” section.

4.7. Effects on ability to drive vehicles and use machines

Effects on ability to drive and operate machinery are not known. Therefore, action must be taken according to the response of the person, during the use of drug.

4.8. Undesirable effects

Very common ($\geq 1/10$); common ($\geq 1/100$ to $< 1/10$); uncommon ($\geq 1/1.000$ to $< 1/100$); rare ($\geq 1/10.000$ to $< 1/1.000$); very rare ($< 1/10.000$); unknown (unpredictable with the available data).

Immune system disorders

Uncommon: Allergic reactions (for example, rashes, swelling in the face, difficulty in breathing, itching), fever

Very rare: Anaphylactic reactions, leading to shock

Nervous system disorders

Uncommon: Headache

Gastrointestinal diseases

Uncommon: Nausea, abdominal pain, vomiting, diarrhea

General disorders and administration site conditions

Uncommon: Fatigue

Investigations

Uncommon: Temporary elevations in serum aminotransferase levels.

Reporting of suspected adverse effects

Post-marketing reporting of suspected drug adverse effects is of major significance. Reporting allows continuous monitoring of the risk/benefit ratio for a particular drug. Health care professionals are required to report any adverse reactions to TÜFAM (Turkish Pharmacovigilance Center) (www.titck.gov.tr; e-mail: tufam@titck.gov.tr; tel : 0 800 314 00 08; faks: 0 312 218 35 99)

4.9. Overdose and treatment

Until today, no cases of toxicity has been reported in humans. Has no specific antidote. In case of overdose, gastric lavage is employed and symptomatic and supportive treatment is applied.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Mucolytic, expectorant

ATC code: R05CB06

Since thick and sticky nature of mucus prevents clearance in some respiratory tract conditions, it causes cough and respiratory problems. Ambroxol dilutes mucus by disintegrating mucoproteins and normalizes secretion. It has been shown that it increased the synthesis of surfactants by stimulating Type II cells in lungs. As a result, by promoting normal operation of ciliary vibratile and easy discharge of sputum, it removes respiratory distress and reduces cough.

5.2. Pharmacokinetic properties

General properties

Ambroxol is the metabolite of bromhexine, which is a substance with expectorant action.

Absorption: When administered orally, it is rapidly and completely metabolized.

Distribution: When administered in fasting conditions, it achieves maximum blood concentration within 2.5 hours. Therapeutical blood concentration is 30 ng/ml. During maintenance therapy, a blood concentration of 50 ng/ml is preserved yet it does not accumulate in body. It binds to plasma proteins at a rate of 90%. Ambroxol passes to cerebrospinal fluid and placenta and is detected in breastmilk.

Biotransformation: Due to first-pass effect in the liver, it is metabolized by one-third. Major enzyme responsible for ambroxol metabolism in liver is CYP3A4. During this process renally excreted metabolites (for example, dibromo antranilic acid, glucuronide) are formed.

Elimination: By extensive metabolization, 90% is excreted in the form of glucuronides and 10 % in the form of unchanged drug, almost completely with urine. Half life is approximately 9-10 hours. The plasma half-life of ambroxol and its metabolites, is approximately 22 hours. Due to high protein-binding rate and distribution volume and due to slow redistribution from tissues, significant elimination of ambroxol with dialysis or forced diuresis, is not expected.

Characteristics in patients

Renal failure: In severe kidney failure, the elimination half lives of ambroxol metabolites are longer.

Hepatic failure: In case of severe hepatic conditions, ambroxol clearance decreases by 20% to 40%.

5.3. Pre-clinical safety data

Acute toxicity

No special sensitivity was seen in acute toxicity studies in test animals.

Chronic toxicity/Subchronic toxicity

In chronic toxicity studies, conducted on 2 species of animals, no changes, connected to the substance, were seen.

Mutagenicity and tumor formation potential

In long-term studies, conducted on test animals, no evidence concerning tumor formation potential of ambroxol, has been shown.

Detailed mutagenicity tests with ambroxol have not been conducted. Studies until today have yielded negative results.

Reproductive toxicity

In embryotoxicity studies, conducted on rats and island rabbits, no evidence for teratogenic potential has been seen in doses up to 3 g/kg and 200 mg/kg. Peri- and post-natal development in rats has been impaired only at a dose over 500 mg/kg.

In rats, fertility disorders have not been observed at doses up to 1.5 g/kg.

Ambroxol passes through placenta barrier and is excreted in animal breastmilk.

6. PHARMACEUTICAL CHARACTERISTICS

6.1. List of excipients

Sorbitol 70% solution (E420)

Glycerine

Propylene glycol

Hydroxyethylcellulose 4000

Benzoic acid

Citric acid monohydrate

Sodium saccharin

Raspberry flavor

Demineralized water q.s.

6.2. Incompatibilities

No data.

6.3. Shelf-life

24 months.

6.4. Special warnings for storage

Store at room temperature below 25°C and in original package.

6.5. Nature and content of the package

Presented in honey-colored bottles with plastic pilfer-proof cap, together with 5 ml spoon.

6.6. The disposal of remnants of human medicinal product and other special precautions

Unused products or waste materials must be disposed in accordance with “Regulation concerning Control of Medical Wastes” and “Regulation concerning Control of Packages and Package Wastes.”

7. MARKETING AUTHORIZATION HOLDER

SANTA FARMA İLAÇ SANAYİ A.Ş.

Okmeydanı, Boru Çiçeği Sok.No.20, 34382 Şişli -İSTANBUL

Tel: (0212) 220 64 00

Fax: (0212) 222 57 59

8. LICENSE NUMBER(S)

188/90

9. DATE OF INITIAL LICENSE/RENEWAL OF LICENSE

Initial license date: 02.10.1998

Date of license renewal: 02.10.2008

10. DATE OF RENEWAL of SmPC
